effect of diazepam and/or droperidol on movement is a more likely possibility. Diazepam acts on spinal cord gamma amino butyric acid (GABA) receptors to enhance presynaptic inhibition and, as a result, reduces release of excitatory transmitter from primary afferents.2 This effect probably accounts for diazepam’s muscle relaxant properties (reduced gain of the stretch reflex) and efficacy in the treatment of spasticity.2 Diazepam also depresses spinal polysynaptic reflexes, but, since higher doses of diazepam are needed to do so in animals with cord transections, this effect apparently depends partially on inhibition of a supraspinal descending facilitory system.2 Moreover, presumably by acting on the spinal cord itself, intrathecally administered benzodiazepines produce analgesia,3,4 and epidural administration may cause weakness. That is, although rats given diazepam epidurally showed no evidence of weakness, accidental epidural administration of diazepam (2 mg) to a patient was associated with profound weakness and sensory blockade.5 Droperidol also has spinal neurochemical effects which could influence movement. It is a weak alpha adrenergic and dopaminergic antagonist and, as demonstrated electrophysiologically and behaviorally, these neurotransmitters are involved in motor responses.5,6 In addition, neuroleptic binding sites exist in the spinal cord dorsal horn, and there is evidence that some neuroleptics act directly on motor neurons to reduce motor output.6 Thus, we speculate that the weakness our patient experienced during tracheal intubation reflects a neurochemical effect of diazepam and/or droperidol on spinal or supraspinal neuronal circuits subserving movement. For this effect to become manifest clinically is evidently rare, and probably depends on the dose and route of drug administration (oral diazepam alone did not worsen our patient’s weakness), and probably requires the coexistence of other as yet undefined conditions (e.g., increased drug access due to an altered blood-spinal cord barrier, or already severely compromised spinal cord function). Consequently, we do not believe one case of this sort warrants abandoning diazepam and droperidol for “awake” tracheal intubation. We do recommend, however, that a neurologic examination be performed after sedation, but prior to intubation, so that drug-induced weakness will not subsequently be confused with neck movement-related cord injury. Clinically, however, it is most essential to recognize that, if a spinal neurologic deficit occurs during sedation or intubation of a patient at risk, one must initially assume it is due to a more serious and potentially correctable problem, such as hypotension or neck hyper-extension, and act accordingly.

REFERENCES


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Accidental Injection of Epidural Methohexital


Occasional reports have appeared describing mistaken administration of drugs into the epidural space.1–3 We describe the accidental injection of 1% methohexital via an epidural catheter.

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CASE REPORT

A 25-yr-old, 63-kg woman was to undergo laparotomy for suspected massive ovarian tumor. She was ASA class I with no significant past medical history. Apart from abdominal distension, physical and labo-
Steen and Michenfelder refer to the possibility of complications arising from inadvertent epidural injections as being related, in part, to the osmolarity of the solution injected. We, therefore, measured the osmolarity of solutions of methohexitol (1% and 5%) and thiopental (2.5% and 5%) when mixed with water. Methohexitol 1% had an osmolarity of 167 mosmol/l; 5% was 493 mosmol/l. Thiopental 2.5% and 5% had osmolarities of 416 and 733 mosmol/l, respectively. The higher osmolarity of more concentrated solutions could explain why the intra-arterial or extravascular injections of, for example, 10% thiopental produces far more serious side effects when compared with the 2.5% solution used today. Permanent and serious sequelae have not been reported to follow intravascular injection. Likewise, the injection of 2% thiopental epidurally was not followed by neurological complications.

The dilemma faced by anesthesiologists following an accidental epidural drug administration is deciding the best course of corrective action. Possibilities include: 1) no further action; 2) dilution of the drug within the epidural space; 3) administration of steroids; and 4) enhancement of the dispersion and absorption of the drug by the use of hyaluronidase. The lack of information on the effects of accidental epidural injections, and the appropriate therapeutic responses, means that whatever clinical course is undertaken will be primarily a decision based upon individual judgement.

Certain knowledge that the drug and its concentration would be harmless would argue in favor of no further action. Such would be the case of a non-toxic drug in low concentrations. It is possible that 1% methohexital is itself non-toxic. The argument for straightforward dilution is that it is the simplest and most direct way to lower the local concentration of drug. The risk involved with dilution is the possibility of spreading toxic effects to higher segments. The risks of nerve damage due to the hyperosmolarity of a smaller volume of solution must be weighed against the potential of more widespread direct toxic effects of a diluted but larger volume.

Bromage believes that corticosteroids, if given early, may be helpful in limiting reactive edema. Based on the frequency of uncomplicated epidural administration of steroids for the treatment of back pain, their prophylactic use after mistaken epidural injection is reasonable.

Hyaluronidase is a soluble enzyme product prepared from mammalian testes. It hydrolyzes hyaluronic acid, an important constituent of intercellular cement, by splitting the glucosaminidic bond between C1 of the glucosamine and C4 of the glucuronic acid. This temporarily decreases the viscosity of the intercellular cement, promotes diffusion, and facilitates absorption of

**DISCUSSION**

Those drugs which have previously been reported as being accidentally administered epidurally include diazepam, 2% thiopental, varying concentrations of potassium chloride (KCl) solutions, colloidon, and hypertonic saline. Almost certainly, many other agents have been accidentally inserted in the epidural space without description of their effects. Bromage makes the point that the epidural space appears to be relatively tolerant of abuse, in view of the startlingly inappropriate solutions having been erroneously injected into it without apparent harm. Nevertheless, there have been tragedies, and paraplegia has arisen from the injection of epidural colloidon, hypertonic saline, and 2% hexylaine, an older local anesthetic drug. Permanent neurological sequelae have not followed the administration of diazepam 0.5% (commercially prepared in a propylene glycol-ethanol-water mixture), 2% thiopental, 6.44% KCl, or, in this case, 1% methohexital.

Surgical examinations were normal. She received diazepam 5 mg orally 90 min before surgery. On arrival in the operating room, an epidural catheter was inserted 5 cm at the L1-L2 interspace. After a test dose of 3 ml 0.5% bupivacaine with epinephrine 1/200,000, 10 ml 2% lidocaine was given. With the onset of detectable sensory blockade, general anesthesia was induced with sufentanil 20 μg, methohexitol 80 mg, and atracurium 25 mg iv. Ventilation was controlled with 60% nitrous oxide in oxygen, and the trachea intubated. Surgery proceeded uneventfully, until the resident administering anesthesia was briefly relieved by another resident. The relieving resident mistakenly administered 5 ml of 1% methohexital via the epidural catheter instead of lidocaine 2%. The mistake was immediately recognized. The course of action chosen was to administer 10 ml preservative-free normal saline as a diluent, followed by 10 ml normal saline containing 40 mg methylprednisolone and an additional 10 ml NS containing 300 units of hyaluronidase. Surgery lasted 2 h, during which no further drugs were administered. The patient awakened, and the trachea was extubated in the operating room. During the transfer to the recovery room, she became somnolent with shallow respirations. Nalbuphine 5 mg was given iv to antagonize residual sufentanil-induced narcosis. While respiratory rate remained 12–16 breaths/min and arterial oxygen saturation greater than 97%, the patient remained sleepy. Ten minutes after arrival in the recovery room, the patient was able to wiggle her toes and grip bilaterally on command. Thirty minutes later, she was mostly arousable. After 1 h in recovery, the patient was able to straight leg raise bilaterally, and was complaining of abdominal pain. A complete neurological examination at this time was normal. Because of her complaint of abdominal pain, 75 μg of fentanyl with 4 mg of morphine was given epidurally. Ten minutes later, she was pain free, with a zone of hypalgesia to T4. The day following surgery, neurological examination was again normal. The epidural catheter was removed at this time after a further epidural dose of morphine 5 mg. The patient had good analgesia, and mild pruritis was relieved by occasional im injections of nalbuphine 5 mg. Daily neurological examinations were normal, and she was discharged on the 5th postoperative day. No delayed sequelae were detectable at a follow-up visit 1 month after surgery. The only effect we could possibly attribute to the epidural injection of methohexitol was the patient’s greater-than-anticipated sleepiness for the first 30 min in the recovery room.
injected drugs or fluids. Sensitivity occurs infrequently, and a sensitivity test just prior to use has been advised.\(^9\) Hyaluronic acid has been studied as an adjuvant for epidural analgesia.\(^10\) The use of 125 units of hyaluronic acid in 25 ml 2% lidocaine with epinephrine 1/200,000 was associated with a decrease in both intensity and duration of neural blockade. In fact, the quality of analgesia with hyaluronic acid was inadequate for surgery. This study demonstrated that hyaluronic acid, rather than enhancing neural uptake of drugs from the epidural space, effected a dramatic reduction of concentration of local anesthetic at its spinal site of action. The effect of hyaluronic acid on increasing the overall vascular uptake of a drug has been amply demonstrated by Mushin.\(^11\) He showed that intramuscular gallamine with hyaluronic acid had a five-fold faster onset time with double the intensity of neuromuscular block than the equivalent injection of gallamine without hyaluronic acid.

In conclusion, accidental drug administration into the epidural space is a rare problem which has caused severe neurological damage. We describe a case in which no neurologic sequelae followed a mistaken epidural administration of 1% methohexital. Treatment consisted of dilution in combination with steroid and hyaluronic acid administration, the effectiveness of which is impossible to evaluate.

References


Air Embolism Associated with Veno-venous Bypass during Orthotopic Liver Transplantation

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Prior to 1982, the anhepatic phase of orthotopic liver transplantation (OLT) was performed by cross-clamping the inferior vena cava (IVC) and portal vein. This resulted in significantly decreased venous return with subsequent decreases in cardiac output. Concomitantly, the venous pressure in the portal circulation was increased, leading to visceral engorgement and the possibility of bowel ischemia, as well as increased bleeding from the adhesions of previous surgeries. The introduction of non-heparinized veno-venous bypass decreased the morbidity and mortality of OLT by partially restoring the cardiac output and decreasing visceral bleeding.\(^1\) The portal vein and IVC are drained by cannulae which are connected to a centrifugal force pump, and venous flow is returned to the superior vena cava via the left axillary vein (fig. 1).

Liver transplantation is a technically difficult procedure for both surgeons and anesthesiologists; many opportunities for complications present themselves. An incident possibly due to venous air embolism (VAE) resulting in severe hemodynamic deterioration during OLT has previously been described, although not related to veno-venous bypass.\(^2\) We wish to report a case

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